REMARKS

Claims 1-31 are currently pending in this application.

The specification has been amended at the paragraph starting at page 12, line 4 to remove the term "estimated." Support for this amendment can be found in the specification as filed, e.g., on page 31 at line 14 and in Table I, starting at page 38, line 11. The specification has also been amended at the paragraph starting at page 12, line 7, to recite the equation used to calculate the slopes in Figure 4. Support for this amendment can be found at page 45, lines 8-10 of the application as filed. The specification has been further amended at the paragraph starting on page 19, line 4 to correct a typographical error. In particular, the paragraph was amended to more particularly specify that the polynucleotide has a "certain" G-C content. For support, see, e.g., page 22, line 21 to page 23, line 9, and page 9, line 10 to page 10, line 17 of the specification as filed. The specification has also been amended at page 27, line 9 to insert the word "contain." This amendment corrects an obvious typographical error. No new matter has been added by any of the foregoing amendments.

Claims 6 and 12 have been amended to more particularly define coefficient b of the equation recited in those claims. Support for these amendments can be found at page 48, line 7-11 and at page 49, lines 21-22. No new matter has been added by these amendments.

Entry and consideration of the amendments is therefore respectfully requested.

The Objection to the Drawings Have Been Obviated

The Examiner has objected to the drawings for failing to comply with 37 C.F.R. § 1.84(p)(5) because they include a reference sign not included in the description. In particular, Reference No. 213 in Figure 2 is not mentioned in the description. Applicants have submitted with this paper an amended version of Figure 2 which omits Reference No. 213. Applicants believe that this amendment obviates the Examiner's objection, and respectfully request that the objection be withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 6, 7, 9, and 12 have been rejected under 35 U.S.C. § 112, second paragraph, for being indefinite. The Examiner alleges that the claims are vague and indefinite because "*b*" is undefined. Applicants respectfully point out that claims 6 and 12 have been amended to define coefficient *b* as a coefficient optimized for predicting polynucleotide melting temperatures. Support for these amendments can be found at page 48, lines 7-11, and at page 49, lines 21-22. Applicants submit that these amendments obviate the Examiner's rejection for indefiniteness, and respectfully request that the rejection be withdrawn.

The Rejection Under 35 U.S.C. §§ 102(a) and (b) Should Be Withdrawn

Pending claims 1-5, 7, 11, and 16-31 have been rejected under 35 U.S.C. § 102(a) and § 102(b), as anticipated by each of the references of Le Novère (*Bioinformatics* (2001) 17(12):1226), Chen *et al.* (*BioTechniques* (1997) 22(6):1158), and Schütz *et al.* (European Patent Publication No. EP 1 103 910 A1). The Office Action indicates, without elaborating, that each of these references "discloses an algorithm for the calculation of melting temperatures of nucleic acids that is embraced by the claims.... [and] further teaches the use of a computer to run the algorithm." See, in the Office Action, from page 2, line 23 to page 3, line 2; and on page 3 at lines 5-8. In response, Applicants respectfully submit that these rejections have been made in error and should be withdrawn. None of the cited references describes or anticipates the presently claimed invention, as explained below.

Anticipation requires that each and every element of the rejected claim(s) be disclosed in a single prior art reference. M.P.E.P. §2131. "A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a simple prior art reference." See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Every element of the claimed invention must be literally present, arranged as in the claim. See *Perkin Elmer Corp. v. Computervision Corp.*, 732, F.2d 888, 894, 221 U.S.P.Q. 669, 673 (Fed. Cir. 1984).

In the present instance the relevant inquiry is not whether a single reference describes an algorithm for calculating the melting temperature of a polynucleotide. The reference must describe

estimating the melting temperature at some desired ion concentration, and it must describe doing this as set forth in the pending claims. To anticipate any of the pending claims, therefore, a single prior art reference must describe modifying some "reference" melting temperature of the polynucleotide by a logarithm of ion concentration ratios, and multiplying that logarithm by a coefficient that is a function of the polynucleotide's G-C content value. See, *e.g.*, step (b) in pending claim 1. As explained in detail below, none of this is described in any of the references cited by the Examiner.

A. Le Novère Does Not Anticipate the Present Invention

Le Novère describes an algorithm, which Le Novère calls "MELTING," that computes the enthalpy and entropy of an oligonucleotide duplex helix-coil transition, and then its melting temperature. This algorithm is also said to include a term, $F([Na+])$, to correct for different salt concentrations. However, this term is not a logarithm of the experimental and "reference" ion concentrations. Nor does Le Novère describe multiplying such a logarithm by any coefficient that is a function of the polynucleotide's G-C content value. Instead, Le Novère simply uses the same correction factor for all oligonucleotides, irrespective of their different sequence and G-C content.

Nor does Le Novère describe limitations set forth in the pending dependent claims. For example, Le Novère does not describe using a coefficient k as specified in dependent claim 3. Nor does Le Novère describe calculating a melting temperature T_m, using a formula specified in dependent claims 4, 6, 10, or 12.

B. The Pending Claims Are Not Anticipated By Chen

Chen *et al.* describes another algorithm, which they call dPrimer, for the calculation of melting temperatures of degenerate oligonucleotides based on the nearest-neighbor model. See Chen, at lines 4-7 of the Abstract on page 1158. In equation 2, on page 1159, Chen indicates that a correction term is to be used that is simply the log of the experimental salt concentration.

However, the correction term in Chen is not multiplied by a coefficient that is a function of the polynucleotide's G-C content value. Like Le Novère, therefore, Chen uses the same correction factor for every oligonucleotide, without accounting for variations in the sequences or

their G-C content. For the reasons above, Chen *et al.* cannot anticipate the pending claims of this application.

C. The European Patent of Schütz Does Not Anticipate This Invention

Schütz (EP 1103910 A1) suffers from the same deficiencies as the Le Novère and Chen references, discussed *supra*, and so also cannot anticipate the invention claimed in this application. In particular, Schütz describes methods (in paragraphs 0034 and 0056) which use a traditional "nearest-neighbor model" to calculate melting temperatures for an oligonucleotide. Schütz also describes a method for adjusting the entropy term, $\Delta S°$, in that algorithm for different concentrations of sodium cations. See, *e.g.*, equation 5 in paragraph 0044 at page 6 of Schütz. However, like the algorithms of Le Novère and Chen, the algorithm does not multiply the logarithm with a coefficient that is a function of the polynucleotide's G-C content. Like Le Novère and Chen, Schütz uses the same correction factor for every oligonucleotide, irrespective of its particular sequence or G-C content value. Hence, Schütz also fails to anticipate any of the pending claims.

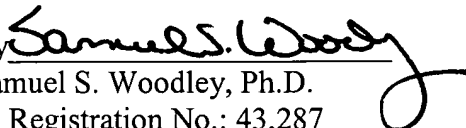### The Objection to Claims 8, 10, and 13-15 Have Been Obviated

Applicants note, with appreciation, that the Examiner has found the subject matter of claims 8, 10, and 13-15 to be allowable. However, the Examiner has objected to these claims because they depend from base claims which have been rejected in the Office Action. The Office Action indicates that claim 8, 10, and 13-15 would be allowable if rewritten in independent form. Applicants believe that the rejection of the base claims have been obviated and should be withdrawn, for the reasons explained above. Applicants therefore respectfully decline to rewrite claims 8, 10, and 13-15, and respectfully submit that the Examiner's objections to those claims have also been obviated and should be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Respectfully submitted,

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By _Samuel S. Woodley_

Samuel S. Woodley, Ph.D.
   Registration No.: 43,287
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 753-6237 (Fax)
Attorneys/Agents For Applicant

Attachments

AMENDMENTS TO THE DRAWINGS

The attached sheet(s) of drawings includes changes to Fig. 2

Attachment: Replacement sheet